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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/656,623	09/04/2003	Raju Kucherlapati	Cell 4.8 CON	7984

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	PAPER NUMBER
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/656,623	KUCHERLAPATI ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7-9,11-13,15-21,23,24,26,34-39 and 46-99* is/are pending in the application.

4a) Of the above claim(s) *1,3-5,7-9,11-13,15-18,21,23,24,35-39 and 46-99* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19,20,26 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response to the restriction requirement received on 12/21/06 has been entered. Claims 1, 3-5, 7-9, 11-13, 15-21,23-24, 26, 34-39, and 46-99 are currently pending in the instant application.

Applicant's election without traverse of Group VIII and the species "IL-6" is acknowledged. Based on applicant's election, Claims 1, 3-5, 7-9, 11-13, 15-18, 21, 23-24, 35-39, and 46-99 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and/or species, there being no allowable generic or linking claim. Therefore, claims 19-20, 26, and 34 are currently under examination. An action on the merits follows.

Priority

The applicant has filed an Application Data Sheet that provides list of applications to which this application claims benefit of priority. It is noted the status is missing for each application. In particular, a number of these applications have issued as Patents. It is suggested that applicant either file a new Application Data Sheet which includes the status of the parent applications, or amend the first page of the specification to include a paragraph setting forth the priority information, including current status.

The disclosure of the prior-filed applications, Application Nos. 07/466,008, 07/610,515, 07/919,297, 08/031,801, and 08/112,848, fails to provide adequate support or enablement in the

manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The claims under consideration recite an immunoglobulin with a fully human variable region specific for IL-6. However, none of the specifications of Application Nos. 07/466,008, 07/610,515, 07/919,297, 08/031,801, or 08/112,848 provide any disclosure for an immunoglobulin with a fully human variable region specific for IL-6, or suggest making such an antibody using transgenic mice as disclosed in any of these parent applications.

The applicant is reminded that in order to receive benefit of priority to an earlier filed application, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). Based on the analysis provided above, none of Application Nos. 07/466,008, 07/610,515, 07/919,297, 08/031,801, or 08/112,848 meet these requirements. Therefore, benefit of priority is denied to Application Nos. 07/466,008, 07/610,515, 07/919,297, 08/031,801, and 08/112,848.

The effective filing date for claims 19-20 and 26 of the instant application is therefore the filing date of parent application 08/234,145, which is 4/28/94.

For claim 34, it is further noted that the 08/234,145 application does not disclose an immunoglobulin analog which is a single chain Fv. As such, the effective filing date for claim 34 of the instant application is the filing date of parent application 08/430,928, which is 4/27/95.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 19-20 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,559,012 (1996), hereafter referred to as Brailly et al., in view of U.S. Patent No. 5,545,806 (1996), hereafter referred to as Lonberg et al. The applicant claims an immunoglobulin with a fully human variable region specific for IL-6,, or for human IL-6. Please note that while claims 19-20 are product-by-process claims, case law states that "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious

from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

Brailly et al. teaches monoclonal antibodies specific for human IL-6, where the antibody is preferably humanized (Brailly et al., columns 1-3). In particular, Brailly et al. teaches that the use of humanized antibodies is advantageous over mouse antibodies in order to reduce the immunogenicity of the antibody in humans (Brailly et al., column 3). In addition, while Brailly et al. does not specifically teach a fully human antibody or an antibody with a fully human variable region specific for human IL-6, Brailly et al. does suggest the use of a fully human antibody derived from a human B cell clone or from in vivo recombination of the genes of the human immunoglobulin repertoire (Brailly et al., column 3, lines 32-37).

Lonberg et al .supplements Brailly et al. by teaching transgenic mice comprising unrearranged human heavy chain and light chain loci, which are capable of producing fully human antibodies following immunization with an antigen (Lonberg et al., claims 1-14, and columns 3-4 and 9-10). In particular, Lonberg et al. teaches the production of human antibodies against human proteins using the transgenic mice (Lonberg et al., columns 9-10).

Therefore, based on motivation provided by the teachings of Brailly et al. for making antibodies against human IL-6 using in vivo recombination of the genes of the human immunoglobulin repertoire, it would have been *prima facie* obvious to the skilled artisan at the time of filing to immunize the transgenic mice of Lonberg et al. with human IL-6 in order to produce a human antibody specific for human IL-6. Further, based on the substantial guidance for making human antibodies in transgenic mice provided by Lonberg et al., the skilled artisan

would have had a reasonable expectation of success in generating a fully human antibody specific for human IL-6 by immunizing the transgenic mice taught by Lonberg et al.

Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,559,012 (1996), hereafter referred to as Brailly et al., in view of U.S. Patent No. 5,545,806 (1996), hereafter referred to as Lonberg et al., as applied to claims 19-20 and 26 above, and further in view of Bird et al. (1988) Science, Vol. 242, 243-246. The applicant claims an immunoglobulin analog with a fully human variable region specific human IL-6, where the analog is a single chain Fv.

As discussed above, Brailly et al. in view of Lonberg et al. provides the teachings and motivation for making a human antibody specific for human IL-6. However, while Brailly et al. and Lonberg et al. discuss antibody fragments/analogs, neither reference specifically teaches or suggests producing a single chain Fv human antibody specific for human IL-6.

Bird et al. supplements Brailly et al. and Lonberg et al. by providing specific guidance for making a single chain Fv for any particular antibody and further provides motivation for making and using single chain Fv by teaching that they have clinical advantages over monoclonal antibodies or Fab fragments (Bird et al., pages 424 and 426). Specifically, Bird et al. teaches that scFv should have lower background in imaging applications, should be less immunogenic, and should penetrate tissues better due to their small size (Bird et al., page 426). In addition, Bird et al. provides a reasonable expectation of success in making an scFV for any antibody by stating, "[w]e are confident that we can produce active single-chain antigen-binding proteins with the sequence of any monoclonal antibody" (Bird et al., page 425, column 3).

Therefore based on the advantages of scFV over monoclonal antibodies taught by Bird et al., it would have been *prima facie* obvious to the skilled artisan at the time of filing to immunize transgenic mice according to Lonberg et al. to produce B cells expressing human monoclonal antibodies against IL-6 as suggested by Brailly et al. and further to prepare scFV of those antibodies using the techniques of Bird et al. with a reasonable expectation of success.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 19-20, 26, and 34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 19-20 and 26-27 of copending Application No. 10/658,521. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

The claims of the '521 application represent a species of the instant claims, as the instant claims are broadly drawn to an immunoglobulin with a fully human variable region, while the '521 claims are drawn to fully human immunoglobulins, which comprise fully human variable and constant regions. It is well established that a species of a claimed invention renders the genus obvious. *In re Schaumann* , 572 F.2d 312, 197 USPQ 5 (CCPA 1978). Thus, claims 19-20 and 26-27 render obvious claims 19-20, 26, and 34 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197.

Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER